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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/586,744	06/02/2000	John Joseph Harrington	9584-0017-999	7865

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EXAMINER	
SAIDHA, TEKCHAND	

ART UNIT	PAPER NUMBER
1652	37

DATE MAILED: 11/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/586744	Harrington et al
Examiner	**Group Art Unit**
T. Saidha	1652

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

P ri d f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 8/13/03 (RCE).

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disp sition of Claims

☒ Claim(s) 1-6, 21-35 & 51-73 ~~is~~/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ ~~is/are allowed.~~

☒ Claim(s) 1-6, 21-35 & 51-73 ~~is~~/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachm nt(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Acti n Summary

Detailed Action

1. Applicants' Request for Continued Examination (RCE) under 37 CFR 1.114 (Paper No. 34-35) based on Application No. 09/586744 is acceptable and a RCE has been established. An action on the RCE follows.

2. The amendment filed 8.13.03 (Paper No. 36) proposes amendments to claims that do not comply with 37 CFR 1.173(b), which sets forth the manner of making amendments in reissue applications. A supplemental paper correctly amending the reissue application is required.

Applicant is notified that any subsequent amendment to the specification and/or claims must comply with 37 CFR 1.173(b). Example, using a status identifier for each claim in parentheses after number, (for example, make changes relative to issue US patent. For example, claim 21 didn't issue in US patent. It should be presented in clean copy, all underlined. Amdts to claim 21 may be presented for examiner's consideration, as marked up copy, with underlines and brackets relative to last amdt, but version entered into case needs to reflect changes made since patent issued.)

3. Claims 1-6, 21-35 & 51-73 are pending and under consideration in this examination.

4. Any objection or rejection of record which is not expressly repeated in this Office Action has been overcome by Applicant's response and withdrawn.

5. Applicants letter filed 3.11.03 (Paper No. 32) and Offer to Surrender Patent is also acknowledged.

The original patent, or a statement as to loss or inaccessibility of the original patent, must be received before this reissue application can be allowed. See 37 CFR 1.178.

6. Applicant's arguments filed as per the amendment cited above have been fully considered but they are not deemed to be persuasive. The reasons are discussed following the rejection(s).

7. The reissue oath/declaration filed with this application is defective because it fails to identify at least one error which is relied upon to support the reissue application. See 37 CFR 1.175(a)(1) and MPEP § 1414.

The reissue oath/declaration filed with this application is defective because the error which is relied upon to support the reissue application is not an error upon which a reissue can be based. See 37 CFR 1.175(a)(1) and MPEP § 1414.

The nature of the defect(s) is that the 'error is not specific, nor is it an error correctable by re-issue'.

In accordance with 37 CFR 1.175(b)(1), a supplemental reissue oath/declaration under 37 CFR 1.175(b)(1) must be received before this reissue application can be allowed.

Claims 1-6, 21-35 & 51-73 are rejected as being based upon a defective oath/declaration under 35 U.S.C. 251. See 37 CFR 1.175. The nature of the defect is set forth above.

Receipt of an appropriate supplemental oath/declaration under 37 CFR 1.175(b)(1) will overcome this rejection under 35 U.S.C. 251. An example of acceptable language to be used in the supplemental oath/declaration is as follows:

> "Every error in the patent which was corrected in the present reissue application, and is not covered by a prior oath/declaration submitted in this application, arose without any deceptive intention on the part of the applicant."

8. ***New Matter***

Claims 21-35 & 51-73 are rejected under 35 U.S.C. 251 as being based upon new matter added to the patent for which reissue is sought.

Applicant argue that 'It is well settled that amendments that replace subject matter incorporated into an application by reference with the **actual text and figures** of the incorporated document do not constitute new matter See, e.g., M.P.E.P 2163.07 (b).

By Applicants own arguments, it is acknowledged that replacing subject matter incorporated into an application by reference with the **actual** text and figures of the incorporated document do not constitute new matter. Therefore incorporation of the actual text or figures from Harrington and Lieber, 1995, J. Biol. Chem. 270 : 4503 would be proper. However, neither the issued patent (U.S.P. 5,874,283) nor the incorporated reference of Harrington and Lieber (1995), describe the method steps of claims 21-35 & 51-73. Applicants may point to the actual text of the referred article of Harrington and Lieber (1995) or the issued patent in overcoming this rejection. There is no support in the instant specification or the incorporated reference that identifies the actual text which would indicate that the invention of claims 21-35 & 51-73 was **conceived at the time of filing this application**. Further there is no basis for methods of cleaving, detecting or formation of a hybridization complex or a kit - where the target nucleic acid having a first or second portion, or where **3'-probe** comprises a 3'-flap region that is 1, 1-10 or 1-20 nucleotides in length (Claims 21-35 & 51-73). It may also be noted that the incorporated reference shows cleaving of the DNA molecule (not RNA) therefore has no basis for 'polynucleotide' cleavage - RNA is not cleaved by FEN-1 (Harrington and Lieber, 1995, see page 1240, column 2, last 2 lines). Similarly there is no basis for 'polynucleotides' or 3' polynucleotides in the claims, whether it is for methods of cleavage or complexes or kits.

Effective incorporation by reference is lacking. Applicants must clearly point out where in specification (or issued patent)or in the properly incorporated reference such methods or complexes have a clear-cut basis, or the invention was conceived at the time of filing this application.

Applicants cite numerous case laws, including *In re Voss*, 194 USPQ 267 (CCPA 1977) *and re Hughe,* 193 USPQ 141 (CCPA 1977). However, since the incorporation of the subject matter is improper, the referenced case laws do not apply.

Applicants' Arguments [previous arguments]:

Applicants misinterpret Examiner's Office Action by stating that 'The Examiner acknowledges these amendments as proper (see Office Action, page 3, lines 9-10), yet at the same time contends Claims 7-73 are based upon new matter'.

In response the Office Action, page 3, lines 9-10 is reproduced here and underlined as follows:

'Therefore incorporation of the actual text or figures from Harrington and Lieber, 1995, J. Biol. Chem. 270 : 4503 would be proper. However, neither the issued patent (U.S.P. 5,874,283) nor the incorporated reference of Harrington and Lieber (1995), describe the method steps of claims 7-73'.

As indicated above the language does not in any way acknowledge that incorporation of the amendment by the applicants was proper - it merely clarifies what the legal standards are and that the incorporation of actual text or figures is acceptable. Applicants clearly missed or ignored the sentence following the underlined statement - which clearly conveys that 'neither the issued patent

(U.S.P. 5,874,283) nor the incorporated reference of Harrington and Lieber (1995), describe the method steps of claims 7-73'.

The issue in all these claims is incorporation of **'3' polynucleotide probe'** in the method step.

Applicants point to Column 11, lines 3-48 and Column 42, lines 63 through Column 43, lines 36 of the issued patent for support or for proper incorporation of actual text.

However, this is not the case, and it can be seen that while cited paragraphs describe the method steps using 5' polynucleotide probe there is no mention of **'3' polynucleotide probe'** in the method steps and therefore the incorporation is improper. Further, no where is the range **'1-10 or 1-20 nucleotides in length'** described or taught.

Further, Applicants' attention is drawn to column 46, lines 65-67 of the issued patent which states that 'no detectable cleavage of 3' flap structure was observed even in the presence of 15 U of FEN-1- which indicates that 3' end is not cleaved' and therefore unsuitable for the method.

Applicants' Arguments (present)

Citing ***In re Rasmussen***, 211 USPQ 323 (CCPA 1981), Applicants argue that "employment of §§ 132 and 112 as interchangeable leads to confusion of two distinct concepts : (1) the adding of new matter to the disclosure; and (2) **broadening of a claim** (Emphasis added).

In response, it is pointed out that 'no scope rejection' under 112 (first) has been made in this Office Action. The rejection made under 35 U.S.C. 112, first paragraph, pertains to subject matter which is not described in the specification (written description), which is distinct from scope or

broadening of claims or enablement rejection under 35 U.S.C. 112, first paragraph. Therefore, no confusion is possible between the two concepts, as argued.

Applicants' arguments that the actual text (and figures) of an incorporated reference may be explicitly amended into the description of a reissue application without violating the 35 U.S.C. § 251 is not persuasive for reasons presented in previous arguments.

9. ***Written Description***

Claims 21-25, 31-35 & 51-68 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The instant claims are directed to a method of detecting the presence of target nucleic acid (claims 21-25 & 31-35), a hybridization complex (claims 51-58) and a kit for detecting the presence of a target nucleic acid (claims 59-68). The instant claims contain no limitations that define the structures of the endonuclease (or FEN-1 SEQ ID NO :) or the strand that FEN-1 uses as substrate, used for cleaving a polynucleotide comprising the 3' and 5' regions or that used in the detection method or for hybridization complex and kit. FEN-1 cleavage is flap strand specific and independent of flap strand length [Harrington & Lieber, 1994, see abstract].

While the specification describes three species of FEN-1 polypeptides - human FEN-1 (SEQ ID NO : 1), murine FEN-1 (SEQ ID NO : 3) and yeast FEN-1 (SEQ ID NO : 5) bearing close sequence homology or the isolation of endonuclease activity RAD2 : SEQ ID NO : 7, calf thymus,

rabbit reticulocytes, etc., but which differ is other respects and is not representative of the entire 'FEN-1' genus. Similarly, description of probe length of 1, 10 or 20 nucleotide is not representative of the range of the nucleotide probe 1-10 or 1-20, as claimed.

Thus there is no disclosure of any particular structure to function/activity relationship in the disclosed species. The specification also fails to describe additional representative species of the polynucleotide probes by any identifying structural characteristics or properties other than the stating that they are capable hybridizing under undescribed conditions and for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

The reasons for the rejection are distinct from that argued by the Applicants or that the Applicants have presented no new arguments than previously addressed.

Arguments :

Applicants argue that the instant application describe a representative number of species of endonucleases adequate to provide written description support for the genus. For example, the disclosure describes three species of FEN-1 polypeptides : human FEN-1 (SEQ ID NO : 1), murine FEN-1 (SEQ ID NO : 3) and yeast FEN-1 (SEQ ID NO : 5). Further species of FEN-1 isolated from nuclear extract of calf thymus, rabbit reticulocytes, Chinese hamster fibroblast, etc., are described. These species adequately represent the genus of suitable endonucleases.

Applicants further argue that amended claims 7-10 & 14-20 describe the cleavage step functionally. Citing case laws in general - *In re Herschler*, 200 USPQ 711 (CCPA 1979); *In re Halleck,* 164 USPQ 647 (CCPA 1970); *In re Fuetterer*, 138 USPQ 217 (CCPA 1963); *In re Boller*, 141 USPQ 740 (CCPA 1964); and *In re Fuetterer* in particular, Applicants argue that a functional description of a genus of salts was held proper in a claim to a composition comprising the salts and other ingredients. In *In re Herschler*, a functional description of a genus of steroids was held proper in a claimed method of enhancing the penetration of a physiologically active steroidal agent across an external barrier membrane of a human or animal subject using an effective amount of DMSO.

In response, and as per the decision affirming in case of *In re Fuetterer*, 138 USPQ 217 (CCPA 1963), the board stated: * * * There is no indication that the function asserted for the salts is known in the art so that the suitable salts could be readily determined without undue experimentation nor is there any criteria given in the disclosure by which it could be fairly readily determined what salts are suitable. It seems that the determination of suitable salts thus would require testing by trial and error many thousands of known salts to ascertain those which would function in the manner required by the claims, and such a burden should not be required of the public or even by those skilled in the art. Accordingly, we will sustain this rejection.

Likewise in the instant case, claims drawn to a method of cleaving a 5'-polynucleotide by FEN-1 does not functionally or structurally define the double flap structure used as substrates in the method [nor are structures well known in the art prior to the instant filing], for being acted upon by the FEN-1 polypeptide, and that the determination of suitable substrates or double flap structures

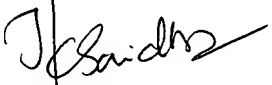
would require testing by trial and error many known or unknown double flap structures to ascertain those which would function in the manner required by the claims, and would involve undue burden upon those skilled in the art.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (703) 305-6595. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group in the Technology Center is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Tekchand Saidha
Primary Examiner, Art Unit 1652
November 14, 2003